REMARKS

Claims 46-91 are pending in the present application. By this amendment, claims 46, 59, 65, 70, 84, and 85 have been amended. Claims 57, 67, 71-81, and 88-90 have previously been indicated as withdrawn from consideration, but Applicants have noted that Claims 72-74 which depend directly or indirectly from Claim 70 were not referred to in the previous Restriction Requirement and are properly examined with Claim 70 which is an elected claim. Applicants submit that claims 46-56, 58-66, 68-70, 72-74 82-87, and 91 are all elected claims and should be currently under examination in the present application. For the reasons set forth below, Applicants submit that the present amendments overcome all prior objections and place this application in condition for immediate allowance.

In the Office Action dated May 12, 2009, the Examiner rejected claims 46-56, 58-66, 68-70, 82-87, and 91 under 35 U.S.C. §103 as being obvious over International Patent Application Publication No. WO 00/55335 of Marasco et al. ("Marasco") in view of Lechmann et al. (2001) Hepatology 34: 4117-423 ("Lechmann") and Ray et al. (2001) FEMS Microbiology Letters 202: 149-156 ("Ray"). Although the Examiner acknowledged that Marasco does not teach or suggest an HCV polyprotein, the Examiner asserted that it would have been obvious to modify the methods of Marasco by using the polyprotein of Lechmann to obtain infectious HCV-like particles. Notwithstanding the specific omission of HCV from the exhaustive list of viruses described in Marasco, the Examiner took the position that Marasco did not include an express exclusion of HCV. The Examiner further asserted that viruses are routinely pseudotyped and that there is not

evidence indicating that one of skill in the art would not have been successful in pseudotyping retroviruses with HCV E1 and E2 proteins. These rejections are traversed for the reasons as stated below.

As an initial matter, by this Amendment, the claims have been amended to make clear that the claimed method makes use of a hepacivirus (HCV) E1 protein and/or E2 protein, wherein the C-terminal transmembrane domain of the E1 and E2 proteins is unmodified with respect to native E1 and E2 proteins. Support for these amendment can be found, at least, on page 8, lines 6-10 of the application-as-filed. As such, all claims now pending refer to production of HCV-like particles using E1 and/or E2 proteins having an unmodified transmembrane domain.

As Applicants pointed out in the application-as-filed, viral particles of the prior art were obtained with chimeric E1 and E2 glycoproteins having transmembrane domains that were modified to allow them to be trafficked to the cell surface. See page 2, lines 8-11 of the application-as-filed. In this regard, Applicants submit further evidence that one of ordinary skill in the art would have understood that pseudotyping was only possible with modified E1 and E2, including the following references submitted herewith: Matsuura et al. (2001) Virology 286: 263-75 ("Matsuura"), and Buonocore et al. (2002) J. Virology 76, 14: 6865-72 ("Buonocore").

As shown in these references, one of ordinary skill in the art at the time of the invention would have understood that HCV E1 and E2 proteins include retention signals in their C-terminal transmembrane domain, which would prevent their expression at the cell surface. See Matsuura, page 264, 1st column, 2nd paragraph; see also Buonocore

(describing modification of HCV E1 and E2 proteins to enable the expression of E1 and E2 proteins at the cell surface).

Accordingly, one of ordinary skill in the art would not have had a reason to combine Marasco, Lechman, and Ray with any reasonable expectation of success in producing HCV-like particles in accordance with the present invention. Indeed, it would have been understood that such pseudotyping was only possible with modified E1 and E2 devoid of retention signals, which would have taught away from the present invention.

Applicants thus submit that the present invention is not rendered obvious by the Marasco, Lechmann, or Ray references, either singly or in combination, and that the claims of the present application relating to a method for producing infectious hepacivirus-like particles are clearly patentable over those references. Applicants thus submit that the Examiner's rejections on the basis of those references is respectfully traversed and should be withdrawn.

In light of the amendments and arguments provided herewith, Applicants submit that all outstanding objections and rejections are overcome, and that the present application has been placed in condition for immediate allowance. Such action is respectfully requested.

Respectfully submitted,

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